<u>AMENDMENTS TO THE SPECIFICATION</u>

Please replace the paragraph starting on page 10, line 12, with the following:

FIGS. [[4a-4b]] <u>4a-4c</u> depict exon profiling of human chromosome 22. FIG. 4a depicts a scanned image of the chromosome 22 exon array hybridized with labeled cDNA derived from RNA from a Jurkat cell line. The array contains 25,000 different 60-mer probes which represent 8183 exons on chromosome 22. Probes comprising control sequences as described were synthesized along the perimeter of the array, and in diagonal stripes across the array. 401 is an enlarged view showing binding sites. [[FIG. 4b depicts]] <u>FIGS. 4b-4c depict</u> using expression data from multiple conditions to validate exons and define gene boundaries on chromosome 22. 402 A grayscale version of a pseudo color image showing $\log_{10}$ ~~expression ratios (Red/Green) for each of the exons (x-axis) across the 69 fluor reversed~~ experiments (y-axis). The 15,511 probes representing the 8,183 predicted exons are arranged in a linear fashion across the 33Mb of chromosome 22. The white lines indicate regions that were enlarged to show examples of specific genes. 403 Expanded region showing a known gene (SERPIND1, NM_ 000185). This example demonstrates how co-regulation across diverse experiments can be used to group exons into genes (the vertical white lines show the boundaries predicted by our gene finding algorithm). 404 Expanded region showing a set 13 co-regulated exons from a known gene (G22P1, NM_001469). This example demonstrates the ability to detect false positives made by the Genscan prediction program. 405 Expanded region representing an EVG (Expression Verified Gene) that collapses two Unigene EST clusters (HS.269963 and HS.14587) into a single transcript. 406 Expanded region showing an EVG containing six exons that are part of a novel transcript that is expressed in the testis (Arrows indicate the position of the two experiments involving testis RNA samples).

Please replace the paragraph starting on page 66, line 16, with the following:

The exon expression state of chromosome 22 has been determined for a variety of different human tissues (see Table 2 below). For example, target polynucleotides were obtained by preparing total RNA from two cell lines, a human T lymphocyte cell line (Jurkat, ATCC # TIB-152) and a chronic myelogenous leukemia cell line (K562, ATCC #CCL-243), as described previously (Marton et al., 1998, Nat. Med. 4:1293-1301). Poly-A+ RNA (mRNA) was isolated from each cell line and labeled using reverse transcription primed with a mixture of random 9-mers and d(T)-20 primers as described in the previous section. The

purified cDNA from the Jurkat cell line was coupled to Cy3 dye while the K562 sample was coupled to Cy5 dye using a Cy Dye^{TM} kit (Amersham Pharmacia, Piscataway, N.J., #Q15108). The coupled samples were combined and hybridized to the chromosome 22 exon array as described above. In such manner, mRNA samples from diverse human cell lines and normal and diseased tissues were fluorescently labeled and hybridized in pairs to 69 individual, chromosome 22 exon arrays. FIG. 4a shows the scanned image (Cy-3 channel) of the chromosome 22 exon array hybridized with labeled RNA from a Jurkat cell line. The intensity data were analyzed using a correlation-based algorithm to assemble exons from local regions of genomic sequence into gene groups. The [[upper]] panel (402) of Figure 4b shows a graphical display of the resulting ratio matrix across all 8,183 exons and 69 condition pairs. A gene identification algorithm was developed 1) to identify exons in a local neighborhood that are strongly correlated across condition pairs and then 2) to extend such regions by incorporating other local exons with similar expression behavior. The resultant groups of co-regulated exons constitute both candidate genes and candidate transcripts. The [[lower]] four panels of Figure [[4b]] 4c are expanded regions of the chromosome 22 exon array that demonstrate the ability of our method to confirm the exons and structure of a known gene (403), to identify true positive and false positive exon predictions (404), to merge UniGene clusters into a single gene (405), and to authenticate *ab initio* gene predictions that are not supported by sequence similarity data (406). FIG. 5 shows a graphical representation of the exon expression states of chromosome 22 for the two cell samples.